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TOPIC: Comments on Consumer-Directed Promotion of Regulated Medical Products

In a Notice published in the Federal Register on Sept. 13, 2005, FDA asked for comments on the Consumer-Directed Promotion of Regulated Medical Products. [1] The Notice asked specific questions but also invited comments on any matter of concern. In this submission I have commented on some of the points raised by FDA, and added some additional points. I teach Food and Drug Law, and I recently addressed some of the issues raised by FDA in a law review article, "Heal the Damage: Prescription Drug Consumer Advertisements and Relative Choices." [2] That article provides more background on the reasons for my recommendations. These comments relate to prescription drugs, the topic examined in the law review article. I have also focused on promotion through television advertisements.

In its first general question, the agency asked whether current DTC promotion presents the benefits and risks of using medical products in an accurate, nonmisleading and balanced way. FDA expressed a particular interest in whether paying greater attention to the educational component of the ads would help consumers understand the role drug therapy plays in treating the disease. I believe the educational component needs to be strengthened. I will note below some recommendations that FDA should consider with respect to this general questions and the other issues identified in the Notice.

1. Relative Choices.

The ads for drugs focus on a particular drug as if the only question were whether the named drug was right for the user in terms of the risk of side effects and the existence of the condition. The doctor, though, needs to consider the relative choice to be made and the risks and benefits of different approaches. The doctor may want to make recommendations on alternative treatments, including dietary changes, or the use of other prescription or OTC drugs as the first step. The drug specific-focus of the ads is not geared to making patients aware of the need for advice on the broader perspective. To correct this, the ads should explicitly recognize that the

[1] 70 Federal Register 54054, Docket No. 2005-0354.

[2] 38 Journal of Health Law 1 (2005).

doctor may provide advice on other alternatives, and should include statements such as that your physician may "recommend other appropriate treatments."[3]

2. Comparative DTC Promotion: Contextual Information and Implied Comparisons for Successor Drugs.

The Notice points out that comparative claims are becoming more common in DTC ads and asks if more contextual information is needed about how efficacy is measured, what side effects there are for the various drugs and drug classes, and whether advantages are accompanied by disadvantages.

I think there is a need for more contextual information. While the need for information may vary with different types of claims, I will discuss the category of follow-on drugs, a topic examined in my law review article. This category refers to a drug sold by a company as the patent on an earlier drug is ending. The successor drug may be sold with a name or trade dress that suggests a similarity to the earlier drug, presumably to retain brand loyalty. The new name, though, may indicate in some way that it is better than its predecessor. For example, the name may include "nex" to indicate that is an advance, and the next step, beyond the earlier drug, a pattern illustrated by Nexium and Clarinex. For ads directed at a lay audience, the ads need to make clear the limited way the new drug may differ from the earlier drug, and the extent to which the testing shows any difference.

Nexium is illustrative. Nexium is more effective in healing erosions than its predecessor Prilosec, but Nexium is a higher dose/ higher strength drug than Prilosec. Many consider the two drugs to be essentially identical.[4] While I can only comment as a lay person, it would seem that doctors would ordinarily want patients to use first the lowest dose that works. The higher dose of any drug may have more side-effects, and the inability of a lower dose to work may indicate that the patient has a more serious condition that needs to be checked. If the lower dose works for the patient's condition, there is no extra medical value in having the patient purchase a more expensive drug. The ads for Nexium should have been clear that the effects of the new drug was similar to the earlier purple pill for treating "acid reflux disease," and that only a limited number suffer from the more severe erosive condition for which Nexium has an increased effectiveness. The ads for Nexium should also have indicated that your doctor may recommend use of other alternatives including lower dose acid stoppers as the first course of treatment. Given the dietary connection in causing heartburn, the ads for the various types of heartburn drugs should also be clear in illustrating what "changes in the diet" means [5]

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[3] Heal the Damage, 38 Journal of Health Law 36-37 (citing an AMA Policy Statement and also suggesting other forms of the statement that could be used perhaps on a rotating basis).

[4] See Merrill Goozner, The $800 Million Pill: The Truth about the Cost of New Drugs 222 (2004)(citing the scientist who codiscovered the proton pump mechanism), and Heal the Damage, p. 26-27.

[5] Heal the Damage, 38 Journal of Health Law at 25, and 36-37.

Clarinex, another follow-on drug, had the same active ingredient as its predecessor, Claritan, but, unlike Claritan, it was tested for use for indoor allergies. Clarinex was tested against a placebo, and had not been tested in a comparison with Claritan. The ads should have made clear that the new drug had the same effect for the primary use for seasonal allergies, and had not been tested for the indoor use against the earlier drug with the similar name.[6] The statute call for advertisements to provide information in brief summary not only about the risks of a drug but also about its "effectiveness." [7] Thus, it is appropriate that the DTC ads provide information about the limits of the effectiveness of the drugs. FDA should give adequate attention to this in its revision of the regulations for DTC ads.

3. Disclosing Generic Drug Names Orally in DTC Ads.

Generic names should be stated orally in ads, especially as the patent term ends. The law requires that the generic name be given in printed advertisements and other printed matter. [8] This information enables physicians to recognize the availability of a lower cost alternative with the same active ingredient. Stating the name orally in the ads will help make consumers more aware of a lower cost-alternative when it becomes available.

4. ***Drug Classes and Lack of Comparative Testing,***

Another difficulty that can arise with DTC ads is that the drugs in a certain pharmacologic class may lack any comparative testing. They may all have been tested only against a placebo, and they may make no comparative claim. Physicians may assume that all drugs in a class are the same absent comparative testing.[9] Lay persons, though, watching ads for these drugs on television, are not likely to realize the limits of placebo testing and may misconstrue a drug with complicated claims to treat a serious condition as a claim for a special benefit. To guard against consumer misperception, these drugs may need to state that the drug has not been shown to be better than other drugs in its class.[10]

Another approach that might be considered is to make it clear in the DTC ads the established class to which a drug belongs. FDA has provided for a prominent identification to physicians of a drug's established pharmacologic or therapeutic class in the recent rule revising

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[6] Heal the Damage, 38 Journal of Health Law 23.

[7] 21 U.S.C. 352 (n).

[8] 21 U.S.C. 352 (e)(1)(A). See Heal the Damage, 38 Journal of Health Law 38.

[9] See 2 Cancer Drugs, No Comparative Data, New York Times, C1 (Feb. 26, 2004)(citing FDA Associate Director for Medical Affairs, Dr. Robert Temple).

[10] Heal the Damage, 38 Journal of Health Law 38-39.

prescription drug labeling.[11] FDA believed a prominent disclosure of the class information in the Highlights section of the labeling can give practitioners "important information about what to expect from that product and how it relates to other therapeutic options."[12] If the DTC ads identified the class it would make consumers aware that there are other drugs of the same type which they and their physicians may wish to discuss. It would then be up to the manufacturer to differentiate the drugs within the class, based on approved testing.

It would also be useful to identify the classes of drugs in DTC ads in ways that consumers can more readily understand. The OTC labeling for heartburn drugs provides an example by differentiating among acid reducers and acid stoppers. [13] Under this approach, the DTC ads for Nexium as well as other drugs in the proton pump inhibitor class might be identified as "acid stoppers."

5. Risk-information: Specific Audiences, the Elderly and Newly-Marketed Drugs. The Notice asks a number of questions about ways to ensure that risk information is conveyed clearly to consumers. The Notice recognizes that the consumer audience includes a variety of audiences, including the elderly, and asks about the issues that arise with respect to ads targeted to a specific consumer population or one that reaches them.[14]

I will point out that FDA's revised rule on prescription drug labeling called for specific disclosures on the limits of testing for geriatric use. [15] The main features of these disclosures should be considered for inclusion in DTC ads for drugs targeted at the elderly or that can be expected to be widely used by them. This approach may also provide a model for dealing with ads targeted to other specific audiences.

I will raise another point that relates to risk information. FDA has asked the Institute of Medicine to do a study on the Assessment of the U.S. Drug Safety System. That study is to consider ways to improve the safety testing for drugs.. The study could have ramifications for DTC advertising. Of course, the IOM study is still underway. My point here is that FDA should re-examine the risk-related aspects of DTC advertising in light of the IOM report when it is issued.

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[11]Requirements on Content and Format of Labeling for Human prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3932 (Jan. 24, 2006), issuing 21 CFR 201.57(a)(6).

[12] Id.

[13] Heal the Damage, 38 Journal of Health Law 26; and see OTC Labeling for Prilosec.

[14] 71 Fed. Reg. 54057.

[15] 21 CFR 201.57 (c)(9)(v)8.5, as found at 71 Fed. Reg. 3993 (2006). (It is difficult to follow the numbering system for the FPI).

6. Improving the Provision of Information for Consumers, and Risk Information: Consumer Labeling.

In Question 3, the Notice asks whether changes in the requirements for an adequate provision of information about DTC ads would improve the usefulness of the information for consumers. FDA also asked in the Notice why viewers are not satisfied with the availability of risk information even when risks are stated in the ads. In my view, there simply may be limits to the amount of information that can be absorbed in a broadcast advertisement. The provision of written information to the consumer about the risks is important in helping the comprehension of the risks. Under FDA's Guidance for the ads, one way to meet the "adequate provision" requirement for disclosing risks to consumers is for the television ad to identify a magazine that contains a Consumer-Directed Print Advertisement (CDPA or magazine ad) with risk information[16] This approach puts the burden on the consumer to find the a magazine and buy it, and it is an unfair and unreliable way to ensure that consumers obtain an adequate statement of the drugs risks and benefits. [17] The other means of meeting the adequate provision requirement can present present privacy issues or require consumers to take initiatives such as using the internet or making phone calls to the manufacturer. [18] The most reliable and suitable way to provide additional information to consumers about the risks of advertised drugs is for the manufacturer to be sure that consumers receive consumer (or patient) labeling about the drug when it is dispensed to them. The new regulations should place that obligation on the manufacturers in addition to other measures.

7. ***Content of Consumer Information and Adequacy of Highlight Information***

FDA has recently revised the content and format for physician labeling in a way that seems to be sensible. The preamble to the regulation, though, states a policy on preemption of product liability that links disclosures about risks from advertised drugs to the risks in the Highlights section in the physician labeling.[19] That policy also ties in to a 2004 FDA draft guidance on Consumer-Directed Print Advertisements (CDPA or magazine ads) that provided that after the issuance of the revised rule, only the Highlights section of the risk information need be included in the CDPA.[20] My comment here does not deal with the general question of whether preemption is appropriate. Rather my concern is with whether the FDA's overall policy on the content and source of the risk disclosures to be made to consumers about advertised drugs is too restrictive.

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[16] Guidance for Industry, Consumer-Directed Broadcast Advertisements, Aug. 1999.

[17] Heal the Damage, 38 Journal of Health Law 17 and note 73.

[18]See FDA Consumer-Directed Broadcast Advertisements Guidance, Questions and Answers, p.3 (Aug. 1999)(available at www,fda,gov/cder/guidance/1804q&a.htm)

[19] 71 Federal Register 3922, 3933-36 , (Jan. 24, 2006), issuing 21 CFR 201.56 and 201.57.

[20] FDA Draft Guidance for Industry, Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements, Draft Jan. 2004, p. 6.

Understanding the FDA policy statement on preempton has its complications, but if I follow it in the advertising context, FDA believes product liability claims about a failure to warn in a television drug ad should be preempted if the substance of the warning was included in the physician labeling at any point and if the manufacturer included in the CDPA/magazine ads the information from the Highlights section in the physician labeling about the drug (as translated into lay language).

Under the newly issued regulation, the warning information in the Highlights for the physician labeling contains a summary of the "most clinically significant information" including "information that would affect decisions about whether to prescribe a drug." 21 CFR 201.57(a)(10). Adverse reaction information is to include the "most frequently occurring reactions." 21 CFR 201.57 (a)(11). The Highlights section prominently informs physicians that the full prescribing information is given in the rest of the labeling, labeling which the physician has.

The impact of FDA's new policy would seem to be that the CDPA/ magazine ad needs to give consumers only the information from the Highlights, even though the consumers would not have direct access to the rest of the information about other warnings or adverse reactions. FDA's Jan. 2004 draft guidance on the CDPA/magazine ads recommended that there be a statement reminding consumers that the information is not comprehensive and providing a toll-free telephone number or web address for consumers to obtain additional information.[21] On the other hand, the example of a CDPA/magazine ad on FDA's web page does not include a phone number or web address, and only in the case of side effects does it note that the listing is "not complete" and that your health professional can "discuss a more complete list of side effects." [22] No similar statement is made for warning information. FDA seems to be no longer encouraging the provision of print information on the other warnings and side effects.

In my view, the consumer labeling or CDPA/magazine ad should include, after the Highlights information, the other specific warnings and adverse reaction information (in lay language) found in the full prescribing information (FPI) for physicians. The FPI provides for warnings, in addition to those in the Highlight section, about "clinically significant adverse reactions (including any that are potentially fatal [or] are serious even if infrequent...." 21 CFR 201.57 c (6). The FPI also includes the "overall safety profile of the drug based on the entire safety base," a profile that covers only adverse events for which there is a basis to believe there is a causal relationship. 21 CFR 201.57 c (7).

Since this information is specifically included in the FPI, there would not be uncertainty about what needs to be included. Thus this situation does not involve uncertainty about the criteria for disclosure, the factor that seems to have been a concern for FDA in developing its

[21] See Draft Guidance, supra at page 3.

[22] Example of Fictional Highlights of Prescribing Information, Based on Proposed Physician Labeling Rule, available at www.fda.gov at //cdnas/cderguid/5669high.doc Revised 12/2003.

preemption policy. If additional risk information is included, it should be listed under a category for less frequent or less serious adverse reactions. Thus, consumers would not seem likely to overreact, or to be distracted from the more serious risks. At a more basic level, the extent of risk disclosures reflects views on the role consumers should have in the decision making. I believe this additional risk information should be included in the consumer labeling or CDPA/magazine ads that accompany the DTC ads. If nothing else consumers should be told clearly that the list of warnings and adverse reactions is not complete and the source from which the consumer can get more printed information.

Even when information on side effects is given, the drug manufacturer and FDA may need to provide more than a mere listing. For example, dry mouth, a side effect listed in the example ad on FDA's home page, seems like a mere inconvenience. But from what I heard from a dentist, a lack of saliva can cause teeth to loosen and lead to tooth loss. If that is so, consumers should be made more aware of the seriousness of the effect.

7. ***Improved Enforcement : Prior Review in Extraordinary Cases.***

In Question 6, FDA asks what action the agency should take when companies disseminate violative material to consumers. At present, in case of violations, the agency asks companies to stop using violative materials, and in some cases to run corrective ads. FDA points out that almost all review of ads is post hoc, and that under the statute prior review is permitted only for situations recognized in the regulations as extraordinary. The agency also pointed out that it is a common advertising technique for an ad to present positive scenes of people enjoying the benefits of a drug while risk information is disclosed. The agency asked if techniques like these create barriers to consumer understanding of risk.

I believe techniques like these can distract from an important safety messages and should be restricted. The broader question is whether there are any extraordinary circumstances that can be identified which would justify prior review as a means to prevent violations. Since these ads are directed at lay consumers, there is a greater risk of confusion than occurs with ads directed to physicians. In issuing the new regulations FDA should consider if there are situations that the regulations might designate as extraordinary circumstances. A possible candidate is the situation where a company has repeatedly made advertisements for a drug that violate the statute and regulations in a material way. Another might be a flagrant violation of a safety-related requirement. The difficulties in presenting comparative claims with adequate contextual information may also constitute an extraordinary circumstance, and especially so if the initial ads have inadequacies.[23] In case of disputes FDA may need to provide informal hearings.

FDA will have to develop an adequate record to support this regulation. The statutory requirement for a hearing on the proposed rule adds to the length and burden of this effort.[24]

[23] See Recommendation 2 above.

[24] The rules are subject to formal rulemaking requirements. See 21 USC 352 (n), and 371 (e). In view of the administrative burdens involved in revising the rules, I have recommended that Congress act by statute. 38 Journal of Health Law 41.

Some may also question whether the Constitutional protections for commercial speech will preclude any prior review of drug advertisements. Commercial speech is considered more "hardy" than expressive and political speech, and prior review of commercial speech may be appropriate. [25] The showing needed to uphold the reasonableness of a regulation on extraordinary circumstances under the Administrative Procedure Act may also be sufficient to help satisfy the constitutional requirements.

FDA has undertaken a challenging project. I hope these comments may be of help in addressing these important issues.

Sincerely yours,

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[25] See Virginia State Bd. Of Pharmacy v. Virginia Citizens Consumer Council, 425 U.S. 748, 772, n. 24 (1976). See Pearson v. Shalala, 164 F.3d650, 660 (D.C. Cir.1999) (finding health claims on foods protected by commercial speech, but also providing for FDA review of disclaimers to be used).